ATTACHMENT A
Remarks

Claims 1-3, 5, 8-66, 69-78, 80, 87-89, 94 and 96-109 are pending in the present application. Upon entrance of this Amendment After Final, Applicants have amended claims 1, 5, 8, 9, 11-13, 22, 24, 41, 49, 51, 63, 65, 69-71 and 74. Applicants respectfully submit that the present application is in condition for allowance based on the discussion which follows.

As an initial point, Applicants respectfully submit that this Amendment After Final is appropriate for entry, as the Amendment clarifies issues for appeal and presents the claims in a better condition for allowance or appeal. Specifically, the claim amendments remove subject matter which was the subject of previous written description and enablement rejections, thus removing issues for appeal. Further, as will be discussed below, the claims, as amended, are now in full compliance with the requirements of 35 U.S.C. § 112. Therefore, in accordance with M.P.E.P. § 1207, the Amendment does not necessitate a new search or raise new issues, which requires further consideration or requires undue burden. Accordingly, this Amendment After Final should be entered.

Turning now to the subject of the outstanding Office Action, claim 13 was rejected under 35 U.S.C. § 112, second paragraph which, by this Amendment, Applicants have amended, thereby obviating the rejection.

Claim 41 was rejected under 35 U.S.C. § 112, second paragraph which, by this Amendment, Applicants have amended, thereby obviating the rejection to claim 41.

Claims 1, 3, 8, 9, 14-16, 41, 63, 65, 66, 69 and 70 were rejected under 35 U.S.C. § 112, first paragraph, for allegedly failing to comply with the written description requirement. By this Amendment, Applicants have amended claims 1, 8, 9, 11, 41, 63

and 69 to remove reference to "functional equivalents thereof capable of inhibiting differentiation of the stem cell," thereby obviating the rejection to the claims under 35 U.S.C. § 112, first paragraph (written description requirement).

Claims 3 and 10-13 were rejected under 35 U.S.C. § 112, first paragraph, for failing to provide a written description for the claimed genus of "a ligand of a class III tyrosine kinase receptor." Further, it was alleged that Applicants made no argument in response to this rejection.

Applicants respectfully direct the Examiner's attention to page 4, second full paragraph of the Remarks of the April 20, 2006 Amendment, which traverses the 35 U.S.C. § 112, first paragraph rejection. Furthermore, Applicants respectfully submit that the specification, as filed, provides a sufficient written description, in conjunction with what is known in the art, to fully support the subject matter of claims 3 and 10-13, in accordance with the requirements of 35 U.S.C. § 112. Accordingly, one of ordinary skill in the art would find the present specification as providing an adequate written description for the claimed genus of "a ligand of a class III tyrosine kinase receptor."

Claims 1, 8, 9, 13, 14, 41, 63, 66, 69 and 70 were rejected under 35 U.S.C. § 102(e) as being anticipated by Lindquist et al. (U.S. Patent Publication No. 2004/0014662) (hereinafter "Lindquist"). The Examiner alleges that Lindquist teaches human cells in paragraphs [0020], [0026], [0040], [0045] and [0156] and claims 34, 39 and 51.

Applicants respectfully disagree with the Examiner's allegation that Lindquist anticipates the claimed invention, as Lindquist fails to provide an enabling disclosure with regard to the presently claimed invention. As discussed in the prior Amendment,

filed on April 20, 2006, Lindquist only provides a sufficient enabling disclosure for one of ordinary skill in the art to practice an invention with regard to rat stem cells not human stem cells. Although the Examiner has attempted to refute the previous argument by citing various paragraphs in Lindquist which reference human cells, Lindquist fails to provide an enabling disclosure with regard to practicing the invention in a human subject. Lindquist provides absolutely no test results or any data which would provide any evidence that its method could be applied to human subjects, merely including disclosure exclusively with regard to the use and success of its method in rat stem cells. Differences in stem cells between rats and humans fail to provide any assurance to one of ordinary skill in the art that what is disclosed and provided in the form of data in Lindquist would be applicable in human stem cells. Therefore, in accordance with the holding of Elan Pharm. Inc. v. Mayo Found., 68 USPQ2d 1373 (Fed. Cir. 2003), Lindquist fails to be an anticipatory reference, as Lindquist fails to enable one of ordinary skill in the art to make or carry out the present invention without undue experimentation.

Furthermore, although Lindquist includes textual reference to humans, mere reference to a hope that its method would be applicable to humans does not, in and of itself, provide enablement due to the lack of disclosure with respect to any results of its method for use in human stem cells, and the variability in rat and human physiology and consequent uncertainty that its method would be successful in human stem cells. Further, it should be noted that Lindquist also makes mere textual reference to the use of stem cells derived from a broad range of species, including cows, horses, dogs,

sheep and cats. As with humans, Lindquist fails to provide any evidence that its treatment or method is applicable to stem cells from any of these animals.

Moreover, disclosure of studies in a rat model does not enable one of ordinary skill in the art to practice its method in human subjects due to differences in cell physiology, which is an unpredictable art, with the physiology of stem cells especially being a comparatively new field of research and, therefore, less predictable still. As a result of this lack of predictability, it is unreasonable to expect that the experimental data provided for rat cells in Lindquist may be reasonably applied to any mammal, including humans. As evidence of the inability to extrapolate the Lindquist data to humans, Lindquist showed S1P to cause the rat stem cells to proliferate and differentiate. By contrast, the present inventors show that when applied to human stem cells, S1P prevents differentiation. Therefore, one cannot necessarily extrapolate data in Lindquist to human subjects with any certainty.

Even if, *arguendo*, the disclosure of Lindquist is enabling for human stem cells (and Applicants strongly deny this), Lindquist simply does not disclose the invention defined by the present claims and, therefore, Lindquist fails to anticipate the present invention. Putting aside the issue of species, the present claims are based on the novel and non-obvious discovery that S1P (and other compounds) are able to prevent differentiation of stem cells. By contrast, Lindquist discloses that S1P is capable of stimulating stem cell differentiation.

Furthermore, the preamble language "for inhibiting differentiation of a human stem cell" breathes life into the claimed method and, therefore, provides patentable subject matter for due consideration in examining the claims. In doing so, Applicants

respectfully submit that the claims are novel over Lindquist. It is settled law that the claim preamble must be read in the context of the entire claim. The determination of whether preamble recitations are structural limitations or mere statements of purpose or use "can be resolved only on review of the entirety of the [record] to gain an understanding of what the inventors actually invented and intended to encompass by the claim." Corning Glass Works, 868 F.2d at 1257, 9 USPQ2d at 1966.

In the present case, Applicants have invented a way of inhibiting differentiation of a stem cell. This has the practical advantage of allowing the continuous passage of stem cells such that banks of undifferentiated stem cells may be established. It is, therefore, appropriate that the preamble language in the present claims is considered when construing the claims and comparing the claims with the prior art.

Furthermore, it must be stressed that the present claims are method claims, where the preamble is generally provided greater weight as compared with a product claim. For example, in Jansen v. Rexall Sundown, Inc., 342 F.3d 1329, 1333-34, 68 USPQ2d 1154, 1158 (Fed. Cir. 2003), a claim was directed to a method of treating or preventing pernicious anemia in humans by administering a certain vitamin preparation to "a human in need thereof." The Jansen court held that the preamble is not merely a statement of an effect that may or may not be desired or appreciated, but rather is a statement of the intentional purpose for which the method must be performed. Thus, the claim was properly interpreted to mean that the vitamin preparation must be administered to a human with a recognized need to treat or prevent pernicious anemia.

Applying Jansen to the present case, the preamble of claim 1 ("for inhibiting differentiation of a human stem cell") must be viewed as a statement of the purpose for

which the method must be performed. Lindquist applies S1P to stem cells not for that claimed purpose and, therefore, Lindquist does not disclose each and every feature of claim 1. Therefore, Lindquist fails to anticipate claim 1 under 35 U.S.C. § 102(e).

Furthermore, reliance on the preamble language of the claims in order to overcome prior art will form part of the file wrapper of this case and will be relevant to the future construction of the claims. A "preamble may provide context for the claim construction, particularly, where that preamble's statement of intended use forms the basis for distinguishing the prior art in the patent's prosecution history." Metabolite Labs., Inc. v. Corp. of Am. Holdings, 370 F.3d 1354, 1358-62, 71 USPQ2d 1081, 1084-87 (Fed. Cir. 2004). The patent claim at issue in that case was directed to a two-step method for detecting a deficiency of vitamin B12 or folic acid, involving (i) assaying a body fluid for an "elevated level" of homocysteine, and (ii) "correlating" an "elevated" level with a vitamin deficiency. Metabolite Labs., 370 F.3d at 1358-59, 71 USPQ2d at 1084. The Metabolite court stated that the disputed claim term "correlating" can include comparing with either an unelevated level, as opposed to only an elevated level, because adding the "correlating" step in the claim during prosecution to overcome prior art tied the preamble directly to the "correlating" step. Metabolite Labs., 370 F.3d at 1362, 71 USPQ2d at 1087. The recitation of the intended use of "detecting" a vitamin deficiency in the preamble rendered the claimed invention a method for "detecting" and, thus, was not limited to detecting "elevated" levels. Id.

Further, in Catalina Mktg. Int'l v. Coolsavings.com, Inc., 289 F.3d at 808-09, 62 USPQ2d at 1785, the court found that "[C]lear reliance on the preamble during prosecution to distinguish the claimed invention from the prior art transforms the

preamble into a claim limitation because such reliance indicates use of the preamble to define, in part, the claimed invention".

With reference to the present application, Applicants' reliance on the preamble in prosecution transforms the preamble into a claim limitation, even if it were not so before. When the preamble is considered, Lindquist cannot be considered as anticipating the present method or in any way affecting novelty of the present method.

Further, the present claims are non-obvious over Lindquist. Again, it is emphasized that Lindquist shows that S1P causes adult rat stem cells to proliferate and differentiate, which is the opposite effect found by the Applicants when S1P is applied to human stem cells. A person of ordinary skill in the art, faced with the problem of uncontrolled stem cell differentiation, upon reading Lindquist, would be led to believe that S1P has the effect of stimulating differentiation of stem cells and would be directed in their investigations to assess other molecules. The skilled person would simply not be motivated to use S1P to overcome the problem before them.

The Applicants have unexpectedly discovered that S1P is capable of inhibiting human stem cell differentiation. Use of S1P in this context overcomes a significant problem in the art, such that it is now possible to expand populations of stem cells without a loss of pluripotency.

Based on the foregoing, Applicants respectfully submit that the present claims are not anticipated by or obvious in view of Lindquist.

In view of the foregoing, Applicants respectfully submit that the present application is in condition for allowance.

END REMARKS